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EXAMINER
CHERNYSHEV, OLGA N

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 05/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/066,211	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

1. Claims 1-39 have been cancelled and claims 40-59 have been added as requested in the amendment submitted on September 04, 2002. Claims 40-59 are pending in the instant application.

Claims 40-59 are under examination in the instant office action.

Specification

2. The use of the trademarks has been noted in this application, see page 148, line 8, for example. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Applicant is advised to review the entire text of the instant specification for other possible use of trademarks.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 40-59 are rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility. The instant

application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose a specific biological role for these polynucleotide or encoded protein or their significance to a particular disease, disorder or physiological process, which one would wish to manipulate for a desired clinical effect.

It is clear from the instant application that the protein encoded by the claimed nucleic acid described therein is what is termed an "orphan protein" in the art. The DNA of the instant application has been isolated because of its similarity to a known DNA. There is little doubt that, after complete characterization, this DNA and encoded protein may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion".

The instant claims are drawn to an isolated nucleic acid encoding a polypeptide of as yet undetermined function or biological significance. It is clear from the instant specification that the claimed novel polynucleotide of SEQ ID NO: 57 encodes a polypeptide designated PRO4999, which has sequence similarity to uromodulin, a protein which "is synthesized in the kidney and is the most abundant protein in normal human urine" (page 13, line 3 of the instant specification). PRO4999 nucleic acid sequence is designated "DNA96031-2664" (bottom at page 112 continuing at page 113). Clone DNA96031-2664 was deposited with the ATCC and assigned number 237-PTA (page 104, lines 14-15).

It is further stated in the instant specification that "PRO4999 […] has certain amino acid sequence identity with UROM_HUMAN. Accordingly, it is presently believed that the PRO4999 polypeptide disclosed in the present application is a newly identified member of the uromodulin protein family and may posses one or more biological and/or immunological activities or properties typical of that protein family" (page 68, lines 5-10). Thus, based on the structural similarities to different proteins, UROM_HUMAN of uromodulins family, it has been suggested that the PRO4999 of the instant invention would also possess similar biological activity.

Numerous publications exist on a topic of predicting protein functions from structural similarities or homology to the known proteins. It is well described in the art that amino acid structure cannot necessarily predict the function of the protein: "Knowing the protein structure by itself is insufficient to annotate a number of functional classes and is also insufficient for annotating the specific details of protein function" (see Skolnick et al., Box 2 on page 36 and the whole paper). Moreover, "Structural similarity does not necessarily mean a common evolutionary origin and homologous sequences may evolve into different folds (according to current classification

schemes)" (See Bork et al., Current Opinion in structural Biology, 1998, 8, page 332, first column, second paragraph). Thus, according to the state of the art, functional characteristics of a protein cannot be unequivocally extrapolated from its structural characteristics. Moreover, in the instant case, because at the time of filing the biological significance of uromodulin was unknown ("[t]he function of uromodulin is unknown", page 13, line 6 of the instant specification), one would reasonably conclude that the function of the instant PRO4999 polypeptide encoded by the claimed nucleic acids, which displays sequence identity to the protein of unknown function, appears to be also not specifically disclosed.

The research data presented in the instant specification indicate that PRO4999 of SEQ ID NO: 58 "tested positive as either stimulator[s] or inhibitor[s] of glucose and/or FFA uptake in an assay using primary rat differentiated skeletal muscle (page 143, Example 61). Based on the results of the assay disclosed in the Example 61 it was asserted that the instant PRO4999 polypeptides "would be expected to be useful for the therapeutic treatment of disorders where either the stimulation or inhibition of glucose uptake by skeletal muscle would be beneficial including, for example, diabetes or hyper- or hypo-insulinemia" (top at page 143). However, based on the information supplied in the instant disclosure, one skilled in the art would clearly not know what is the specific utility of the instant PRO4999 nucleic acids with respect to glucose or FFA uptake. The instant specification, as filed, fails to provide any evidence or sound scientific reasoning that would support a conclusion that the instant claimed PRO4999 polynucleotides can be used for the treatment of any pathological condition or disease, including "disorders where either the stimulation or inhibition of glucose uptake by skeletal muscle would be beneficial".

In the absence of knowledge of the biological significance of these specific PRO4999 nucleic acid or encoded protein, there is no immediately obvious patentable use for the claimed polynucleotides. According to the specification of the instant application "[n]ucleotide sequences (or their complements) encoding PRO have various applications in the art of molecular biology, including uses as hybridization probes, in chromosome and gene mapping and in the generation of anti-sense RNA and DNA" (page 82, lines 1-4 of the instant specification). However, it has been well settled that using a polynucleotide sequence as hybridization probe or in chromosome mapping does not support a specific and substantial credible utility for the claimed nucleic acid. Furthermore, to employ the instant PRO4999 polynucleotides in the methods for generation of transgenic animals, as suggested in the instant specification (page 84, lines 10-26, for example) is not a "real world" utility because it would eventually relate to a polynucleotide encoding a protein for which no biological function is known. The instant application also fails to demonstrate use of the polynucleotide of SEQ ID NO: 57 as a marker for any disease or condition (which would be a real world use).

Thus, to employ a polynucleotide PRO4999 of the instant invention in any of the disclosed methods would clearly be using it as the object of further research, which has been determined by the courts to be a utility, which, alone, does not support patentability. Since the instant specification does not disclose a substantial "real world" use for the PRO4999 in their currently available form, then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 40-59 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

5. Claims 40-44 and 55 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 40-44 are directed to nucleic acid molecules having at least 80%, 85%, 90%, 95% or 99% sequence identity with a polynucleotide of SEQ ID NO: 57. Claim 55 is directed to a fragment of at least ten nucleotides that hybridizes to an isolated nucleic acid of SEQ ID NO: 57. The claims do not require that the nucleic acids possess any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polynucleotides that is defined only by sequence identity. However, the instant specification fails to describe the entire genus of nucleic acid molecules, which are encompassed by these claims. In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant has possession of a

nucleic acid molecule which encodes a protein which has the amino acid sequence of SEQ ID NO: 58. This nucleic acid molecule has a nucleic acid sequence of SEQ ID NO: 57 and is contained within ATCC deposit number 237-PTA. The claims are drawn to nucleic acids having at least 80%, 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence or to a fragment of an isolated nucleic acid complementary to a polynucleotide of SEQ ID NO: 57. Thus, the claims are not limited to a polynucleotide with a specific nucleic acid sequence. The claims only require the claimed polynucleotides to share some degree of structural similarity to the isolated nucleic acid of SEQ ID NO: 57. However, the specification only describes a polynucleotide having the nucleic acid sequence of SEQ ID NO: 57 and fails to teach or describe any other polynucleotide which lacks the nucleic acid sequence of SEQ ID NO: 57 and has any relevance to PRO4999.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. The specification does not provide a complete structure of those polynucleotides having at least 80%, 85%, 90%, 95% or 99% sequence identity with a polynucleotide of SEQ ID NO: 57 or fragments of nucleic acid molecules complementary to a polynucleotide of SEQ ID NO: 57 and fails to provide a representative number of species for the claimed genus (those nucleic acids having at least 80%,

85%, 90%, 95% or 99% sequence identity with or fragments of a polynucleotide of SEQ ID NO: 57). Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polynucleotides comprising the nucleic acid sequence set forth in SEQ ID NO: 57, but not the full breadth of the claim meet the written description provision of 35

U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 40-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 40-45, 48-49 and 53 are vague and indefinite for recitation of "extracellular domain" claimed to be shown in Figure 32. However, Figure 32 does not indicate the claimed sequences. Clarification is required.

8. Claim 54 is indefinite and ambiguous for recitation of hybridization "under stringent conditions". Without providing a precise set of hybridization conditions, in the claim or the specification, the metes and bounds of the claimed isolated nucleic acid molecule cannot be defined.

9. Claims 46-47, 50-52 and 55-59 are indefinite for being dependent from indefinite claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 53 and 55 are rejected under 35 U.S.C. 102(b) as being anticipated by Hopp et al., 1991 (US Patent 5,011,912).

Claims 53 and 55 are directed to an isolated nucleic acid that hybridizes to a nucleic acid sequence of SEQ ID NO: 57. Applicant is advised that because claims do not recite a specific set of hybridization conditions under which the claimed polynucleotides are capable of hybridizing to a nucleotide sequence of SEQ ID NO: 57 and because any nucleic acid is capable of hybridizing to any other nucleic acid under some set of hybridization conditions these claims encompass any isolated polynucleotide in existence. An example of such polynucleotides can be found in the publication of Hopp et al., 1991 (see column 7, for example). Thus, document of Hopp et al. anticipates claims 53 and 55.

Conclusion

11. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 872-9306. If this number is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (571) 273-0870. Official papers should NOT be faxed to (571) 273-0870.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Olga N. Chernyshev, Ph.D.

OLGA N. CHERNYSHEV, PH.D.
PATENT EXAMINER